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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/682,595	10/09/2003	Margaret K. Hostetter	110.00580102	1422
26813 7590 01/31/2007 MUETING, RAASCH & GEBHARDT, P.A. P.O. BOX 581415 MINNEAPOLIS, MN 55458			EXAMINER ZEMAN, ROBERT A	
			ART UNIT	PAPER NUMBER
			1645	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/682,595	Applicant(s) HOSTETTER ET AL.	
	Examiner Robert A. Zeman	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-24, 44 and 47-74 is/are pending in the application.
- 4a) Of the above claim(s) 44, 57, 58, 61, 62 and 66-74 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 52 and 56 is/are allowed.
- 6) ☒ Claim(s) 20-24, 47-51, 53-55, 59, 60 and 63-65 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) ☒ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) ☐ Notice of Informal Patent Application |
| 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>2-5-2004</u> . | 6) ☐ Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 1 in the reply filed on 11-6-2006 is acknowledged. The traversal is on the ground(s) that:

- The proteins to which the claimed antibodies bind have been searched in the parent application.
- Claims 59 and 60 should have been included in group I as they depend from claim 22.
- Claim 59 is drawn to an antibody that specifically binds to a protein about 34 kDa from *Streptococcus pneumoniae* hence claim 58 belongs in Group I
- Claims 61 and 62 (group IV) are drawn to chimeric proteins comprising at least one variable domain which specifically binds to a protein comprising at least 80% sequence identity with SEQ ID NO:2 and 66 and 67 (group V) are drawn to compositions comprising at least one antibody variable domain wherein said domain specifically binds to a protein comprising at least 80% sequence identity with SEQ ID NO:2. Since it is well known that a variable domain is portion of an intact antibody, hence said claims should be included in group I.

This is not found persuasive because:

- Each application is searched and examined based on its own merits. Moreover, the elected claims are drawn to antibodies not polypeptides.
- Claims 59 and 60 are rejoined.

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- Contrary to applicant's assertion, claim 59 is drawn to a fragment of an antibody that binds to a protein comprising at least 80% sequence identity with SEQ ID NO:2. Moreover, claim 58 and 50 do not encompass the same antibodies as the proteins they bind to are not necessarily the same. Claim 50 is limited to having at least an 80% sequence identity with SEQ ID NO:2, Claim 58 does not have this constraint. The only similarities required between the proteins the antibodies bind to must share are their molecular weight and a specific function of their binding partners. Consequently, the search of the two compositions would not be coextensive in scope.
- Variable regions of antibodies do not necessarily correlate to an intact antibody as binding domains are used as targeting moieties in multiple compositions. Consequently, the search of the compositions of Group I would not be coextensive in scope with the search of Groups IV or V.
- Applicant's desire for the rejoinder of method claims upon the allowance of the elected claims is noted.

The requirement is still deemed proper and is therefore made FINAL.

Claims 20-24, 44 and 47-74 are pending. Claims 44, 57-58, 61-62 and 66-74 are withdrawn from consideration as being drawn to non-elected inventions. Claims 20-24, 47-56, 59-60 and 63-65 are currently under examination.

Specification

The specification is objected to as it does not reflect the current status of the recited priority applications (i.e. U.S. Patent Application 09/403,422 is now U.S. patent 6,676,943) Appropriate correction is required.

Claim Rejections - 35 USC § 112, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-24, 47-51, 53-55, 59-60 and 63-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to a genus of antibodies, the members of which specifically bind to a protein with at least an 80% sequence identity with SEQ ID NO:2 and wherein said protein binds human complement protein C3. Moreover, the antibodies of claims 47, 55 and 65 must also inhibit the binding of *Streptococcus pneumoniae* to human complement C3 protein.

The courts have recently decided in *Randolph J. Noelle v Seth Lederman, Leonard Chess, and Michael J. Yellin* (CAFC, 02-1187, 1/20/2004) that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species

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because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Enzo Biochem II, 323 F.3d at 965; Regents, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen. Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

In the instant application, Applicant has failed to "fully characterize" the antigen (i.e. proteins with at least 80% sequence identity to SEQ ID NO:2) to which the claimed antibody

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binds. The instant claims are drawn to all antibodies with specificity to any protein with the required sequence identity and that binds human complement protein C3. Consequently, since Applicant has not fully characterized the antigen to which the claimed antibodies bind, the written description requirements under 35 U.S.C 112, first paragraph have not been met.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of specifically bind to a protein with at least an 80% sequence identity with SEQ ID NO:2 and wherein said protein binds human complement protein C3, one must describe the antigenic determinants (immunoepitopes) of the antigen (haemagglutinin peptide) that induces antibodies with the claimed binding specificity.

Aside from SEQ ID NO:2 (and the fragment consisting of residues 1-50 of SEQ ID NO:2), the specification does not describe with any degree of specificity members of the genus of proteins capable of bind human complement C3 to which the members of the claimed genus of antibodies must bind, wherein the case of claims 47, 55, and 65 said antibodies inhibiting the binding of *S. pneumoniae* to human complement C3 protein such that the specification might reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

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Moreover, the specification does not disclose distinguishing and identifying features of a representative number of members of the genus of antibodies to which the claims are drawn, such as a correlation between the structure of the immunoepitope its recited function (specifically binding to a protein with at least an 80% sequence identity with SEQ ID NO:2 and wherein said protein binds human complement protein C3), so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of antibodies. Additionally, the specification fails to disclose which amino acid residues are essential to the function of the immunoepitope or which amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent. Therefore, since the specification fails to adequately describe at least a substantial number of members of the genus of immunoepitopes on which the claims are based; the specification fails to adequately describe at least a substantial number of members of the claimed genus of antibodies.

MPEP § 2163.02 states, “[a]n objective standard for determining compliance with the written description requirement is, ‘does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed’ ”. The courts have decided:

The purpose of the “written description” requirement is broader than to merely explain how to “make and use”; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the “written description” inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable

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from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing

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only one species within the genus” (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by Greenspan et al. (*Nature Biotechnology* 7: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an “epitope” (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that bind antibodies that can prevent biofilm formation can only be identified empirically. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of immunoepitopes, the skilled artisan could not immediately recognize or distinguish members of the claimed genus antibodies with a binding specificity for a protein with at least an 80% sequence identity with SEQ ID NO:2 and wherein said protein binds human complement protein C3. Therefore, because the art is unpredictable, in accordance with the *Guidelines*, the description of immunoepitopes (antigenic determinants) is not deemed representative of the genus of antibodies to which the claims refer.

Claim Rejections - 35 USC § 112, Enablement

Claims 20-24, 47-51, 53-55, 59-60 and 63-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies raised against the full

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length of SEQ ID NO:2 or residues 1-50 of SEQ ID NO:2, does not reasonably provide enablement for any other antibody that specifically binds to a protein with at least an 80% sequence identity with SEQ ID NO:2 and wherein said protein binds human complement protein C3 or any antibody that inhibits the binding of *S. pneumoniae* to human complement C3 protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims without undue experimentation.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

Breadth of the claims

The rejected claims are drawn to a genus of antibodies, the members of which specifically bind to a protein with at least an 80% sequence identity with SEQ ID NO:2 and wherein said protein binds human complement protein C3. Moreover, the antibodies of claims 47, 55 and 65 must also inhibit the binding of *Streptococcus pneumoniae* to human complement C3 protein.

Working Examples/Guidance of Specification

The specification fails to describe immunoepitopes against which the claimed antibodies are raised and must subsequently bind. The working examples disclose specific antibodies that meet the limitations of the instant claims. However, these “examples” are not sufficient to provide enablement for the full scope of the rejected

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claims. Moreover, the specification is silent as to which, if any, immunoepitope confers the ability of a given antibody to inhibit the binding of *S. pneumoniae* to human complement C3 protein.

State of the prior art and Unpredictability of the art

In the instant application, Applicant has failed to “fully characterize” the antigen (i.e. proteins with at least an 80% sequence identity with SEQ ID NO:2 and wherein said protein binds human complement protein C3) to which the claimed antibody binds. The instant claims are drawn to all antibodies with specificity to any protein that has at least 80% sequence identity with SEQ ID NO:2 and binds human complement C3.. Consequently, since Applicant has not fully characterized the antigen to which the claimed antibodies bind, the skilled artisan would not be able to make the claimed invention.

As evidenced by Greenspan et al. (*Nature Biotechnology* 17: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an “epitope” (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically. Even using a competition assay, the skilled artisan cannot determine whether an antibody binds the same epitope as another antibody because an antibody that competes with another does not necessarily bind the same epitope as the other; rather, one antibody may bind a spatially overlapping epitope to sterically hinder binding of the

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other. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of epitopes to which the members of the claimed genus of antibodies must bind, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Consequently, the specification is only enabling for antibodies raised against the full length of SEQ ID NO:2 or residues 1-50 of SEQ ID NO:2.

Conclusion

Claims 20-24, 47-51, 53-55, 59-60 and 63-65 are rejected.

Claims 52 and 56 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866.

The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



ROBERT A. ZEMAN
PRIMARY EXAMINER

January 22, 2007